Exhibit 5

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*721 PATENTING THE HUMAN GENOME [FNa]

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The increasing promise of federal funding for mapping and sequencing the human genome [FN1] has brought with it renewed attention in the research science community to issues of intellectual property protection for products of biotechnology research. Echoing concerns raised a decade ago in the debate over commercialization of academic biomedical research, [FN2] scientists have called for the free availability of all information generated through the Human Genome Project and have argued against allowing private intellectual property rights in such knowledge. [FN3] Meanwhile, private parties have quietly been obtaining patents on bits and pieces of the human genome from the Patent and Trademark Office (PTO). [FN4]

Notwithstanding the willingness of the PTO to issue these patents, the *722 patents may still be vulnerable to challenges to their validity in the courts. Patent claims to human DNA sequences raise unresolved issues under traditional patent doctrine. Moreover, even if the patent claims are valid under existing law, one might question the wisdom of issuing patents on DNA sequences in the human genome to private parties, particularly at a time when the government is devoting public resources to a concerted research effort to generate this information. This Article examines some of these issues.

I. DOCTRINAL IMPEDIMENTS TO PATENT PROTECTION FOR DNA SEQUENCES

A United States patent confers the exclusive right to make, use or sell the patented invention in the United States for a period of seventeen years. [FN5] During the term of the patent, the patent holder has the right to prevent anyone from using the invention -- even an innocent infringer who develops the same invention independently. [FN6] In exchange for these broad exclusive rights, the inventor must disclose the invention to the public in terms that are sufficient to enable others "skilled in the art" to make and use it. [FN7] Judicial decisions characterize the enabling disclosure in the patent as the "quid pro quo" of the patent monopoly. [FN8] In order to obtain a patent, the applicant must first contribute "a measure of worthwhile knowledge to the public storehouse." [FN9]

It is a fundamental axiom of patent law that one may patent only that which is new. Section 101 of the Patent Act defines as patentable subject matter "any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof." [FN10] These categories of statutory subject matter tend to limit patent protection to inventions in fields of applied technology, as opposed to basic scientific *723 research. [FN11] In addition to being new and useful, an invention must satisfy the further statutory requirement of nonobviousness [FN12] to be patentable. One may not obtain a patent by disclosing a claimed "invention" that is already available to the public, whether it is available because it is previously known or because it is readily discoverable through obvious advances over the prior art.

An intuitively appealing objection to patent protection for DNA sequences in the human genome is that the sequences themselves are not new. The human genome resides in every cell of every human being. DNA sequences within this genome exist quite apart from the inventive efforts of the private parties who might seek to patent them, and thus no one may claim to have invented them.

A similar argument persuaded a majority of the Supreme Court in the 1948 case of *Funk Brothers Seed Co. v. Kalo Inoculant Co.* [FN13] The plaintiff in *Funk Brothers* held a patent on a mixed culture of different strains of bacteria, each of which was useful to inoculate the roots of different species of leguminous plants, allowing the plants to fix nitrogen from the air. [FN14] The different species of root-nodule bacteria each existed in nature and had long been available separately in the market, although in the past it had been necessary to buy different inoculants for different crops. Previous efforts at combining the different species of bacteria in a mixed culture suitable for inoculating a range of crops had failed because the different species inhibited each other's effectiveness when combined. The plaintiff's contribution lay in discovering strains of each species of root-nodule bacteria that were not mutually inhibitive and combining these strains in a single mixed-culture inoculant.

***724** Justice Douglas, writing for the majority, held the patent claims to the mixed culture invalid, reasoning that

> patents cannot issue for the discovery of the phenomena of nature . . . . The qualities of these bacteria, like the heat of the sun, electricity, or the qualities of metals, are part of the storehouse of knowledge of all men. They are manifestations of laws of nature, free to all men and reserved exclusively to none. [FN15]

He noted that the patentee created no new bacteria and that the bacteria in the mixed culture "serve the ends nature originally provided and act quite independently of any effort of the patentee." [FN16]

A broad reading of *Funk Brothers* would argue against patent protection for naturally occurring DNA sequences, perhaps even when those sequences are combined with other natural materials to create new recombinant organisms. One could argue that DNA sequences are "manifestations of laws of nature, free to all men and reserved exclusively to none." [FN17] Moreover, much of the impetus for cloning human genes arises from the fact that these genes continue to "serve the ends nature originally provided" when they are expressed in recombinant organisms. The universality of the genetic code ensures that recombinant bacteria can make the same proteins as human cells if they are provided with the right DNA sequences. Thus these human DNA sequences continue to perform their natural functions when they are incorporated in recombinant organisms, just as the different species of root-nodule bacteria continued to perform their natural functions when incorporated in a mixed-culture ***725** inoculant.

Although the *Funk Brothers* decision has never been overruled, in retrospect it seems to represent the high-water mark in the "products of nature" doctrine. Subsequent case law does not deny patent protection to all inventions composed of naturally occurring products or manifesting laws of nature. Instead, the cases suggest that the patentability of such inventions turns on whether the claimed invention is a new product or process resulting from human intervention and, if so, whether the invention is obvious in light of the prior art, including previously available natural products.

A. Patentable Subject Matter and Novelty

The Supreme Court revisited the question of patentability of biotechnology inventions in its 1980 decision in *Diamond v. Chakrabarty.* [FN18] The invention at issue in that case was a living microorganism into which the inventor had introduced multiple naturally occurring bacterial plasmids. These plasmids, or rings of bacterial DNA, contained genetic information that gave the transformed organism the capacity to break down multiple components of crude oil. The patent examiner rejected claims to the bacteria on the alternative grounds that (1) they were "products of nature" and (2) as living organisms they were not within the scope of patentable subject matter. The Patent and Trademark Office concluded that the new bacteria were not "products of nature" because bacteria containing the

multiple plasmids did not occur in nature, [FN19] but nonetheless affirmed the rejection of the claims on the alternative ground that living organisms are not patentable.

On appeal, the Supreme Court held that a living, genetically altered organism may qualify for patent protection as a new "manufacture" or "composition of matter" under section 101 of the Patent Act. [FN20] The Court distinguished *Funk Brothers* on the ground that while the patent holder in that case had not altered the function of any of the species of root-nodule bacteria in the mixed-culture inoculant, Chakrabarty had created ***726** "a new bacterium with markedly different characteristics from any found in nature." [FN21] His discovery was thus "not nature's handiwork, but his own; accordingly it is patentable subject matter . . . . " [FN22] In support of its broad construction of the categories of patentable subject matter, the Court quoted language from the Committee Reports accompanying the 1952 Patent Act to the effect that Congress intended statutory subject matter to "include anything under the sun that is made by man." [FN23]

Under *Chakrabarty,* the relevant inquiry for distinguishing between patentable subject matter and unpatentable products of nature is whether the claimed invention is the result of human intervention. Focusing this inquiry on human DNA sequences, one might still conclude that they should not be patentable as such, although there might be patentable invention in the creation of recombinant materials that incorporate human genes. For example, a scientist who identifies the DNA sequence for a human protein, incorporates the sequence in a recombinant plasmid, and introduces the plasmid into a recombinant bacterial host cell might be able to claim the recombinant plasmid and the transformed host cell as patentable inventions. These recombinant materials do not occur in nature but are the result of human intervention, much like the plasmid-transformed bacteria in *Chakrabarty.* [FN24] On the other hand, the DNA sequence itself, like the bacterial strains in *Funk Brothers,* exists in nature quite apart from the efforts of the inventor and, therefore, should not be patentable ***727** unless it has been altered somehow by human intervention. [FN25]

But even if the claimed DNA sequence is identical to a sequence that exists in nature, it may still fall within the categories of patentable subject matter if the patent applicant has made the sequence available in an isolated or purified form that does not exist in nature. [FN26] A substantial body of case law holds that newly isolated or purified materials may be patented even though those materials exist in nature in an impure state, at least if the purified materials offer some advantage in utility over the naturally-occurring impure materials. [FN27] For example, in *Merck & Co. v. Olin Mathieson Chemical Corp.,* [FN28] the inventors obtained a patent on purified***728** vitamin B_{12} isolated from fermentation materials. Vitamin B_{12} was produced naturally in minute quantities in the livers of cattle and in certain microorganisms. The Fourth Circuit nonetheless upheld the validity of the patent, noting that the patented product was superior to the previously available vitamin B_{12} from cattle because of its relatively abundant supply, cheap price, freedom from toxic substances, and amenability to control of potency and dosage. [FN29] The court called into question the vitality of the "products of nature" doctrine, observing:

> There is nothing in the language of the Act which precludes the issuance of a patent upon a "product of nature" when it is a "new and useful composition of matter" and there is compliance with the specified conditions for patentability. . . . The "matter" of which patentable new and useful compositions are composed necessarily includes naturally existing elements and materials. [FN30]

This language suggests that there is no bar to patenting a "product of nature," assuming the invention is new, useful, falls within the categories of patentable subject matter set forth in section 101, and otherwise satisfies the statutory requirements for patent protection. On the other hand, since the court went to the trouble of pointing out the utilitarian advantages of the purified product over the naturally-occurring impure product, one might conclude that these advantages were important to the court's conclusion that the purified product was a new composition of matter.

In the more recent case of *In re Bergstrom,* the Court of Customs and Patent Appeals rejected the argument that there were impediments to patent protection for "naturally occurring" products beyond those set forth in the patent statute. [FN31] The court reversed a rejection of claims to purified prostaglandins, noting that any differences in the

usefulness or other properties of the purified products compared to the impure materials existing in nature would be relevant only in determining the obviousness of the claimed invention under section 103 and not in determining its status as patentable subject matter under section 101. [FN32] The same court extended ***729** the rationale of the cases upholding the patentability of purified chemicals in *In re Bergy,* [FN33] reversing the rejection of a patent claim to a "biologically pure culture" of a naturally occurring microorganism on the ground that the pure culture did not exist in nature and could be produced only under carefully controlled laboratory conditions. [FN34]

Applying these principles to human DNA sequences, one could argue that a newly cloned human gene that previously existed within the chromosomes of human cells is analogous to a newly isolated or purified chemical that previously existed in impure form. In each case, the inventor has arguably created a new composition of matter by identifying something that previously existed only in combination with other materials and making this new composition more readily accessible for human purposes. Cloned genes are certainly useful in ways that the same DNA sequences found in the chromosomes of human cells are not. Once a gene has been cloned, it may be replicated and expressed in a recombinant host cell, creating numerous copies of the gene for purposes of sequencing and study. Moreover, a cloned gene provides a means of producing its corresponding protein in larger quantities and in a more pure form than may be obtained conveniently from human cells. The cloned gene thus has distinct advantages over the gene as it exists naturally in the chromosomes of human cells, just as purified vitamin B_{12} has distinct advantages over impure vitamin B_{12} as it exists in cow liver.

In sum, while the question remains debatable, newly cloned DNA sequences from the human genome may well be within the range of patentable subject matter as new compositions of matter.

B. Nonobviousness

Even if a claim to a DNA sequence survives a challenge based on lack of patentable subject matter or lack of novelty, it may still be held invalid on the ground that the invention would have been obvious at the time it ***730** was made to a person having ordinary skill in the field in light of the prior art. [FN35] While the novelty requirement asks whether the claimed invention is new, the nonobviousness requirement asks whether the claimed invention represents enough of an advance over the prior art to deserve patent protection. Since the obviousness of an invention is measured against the background of human knowledge at the time the invention is made, this requirement is increasingly difficult to pass as scientific knowledge advances in a field.

The fact that the Patent and Trademark Office has issued patents on some DNA sequences thus does not necessarily portend that such patents will continue to issue in the future. Even without any change in existing law, it is likely that scientific advances in biotechnology and related fields will make future DNA sequences obvious as of the time they are identified. For example, improved cloning techniques and DNA sequencing techniques may render the successful identification of the DNA sequence in a gene of interest routine and predictable. For that matter, advances in protein chemistry that facilitate the separation, purification, and amino acid sequencing of proteins of interest could make the cloning and sequencing of genes corresponding to these proteins a trivial scientific achievement, well within the ordinary skill of biotechnology practitioners.

The courts have sometimes upheld the validity of claims to newly purified chemicals over challenges that they were obvious in light of previously existing impure products. [FN36] Although I have found no court decisions invalidating claims to DNA sequences on grounds of obviousness, the Patent and Trademark Office has rejected such claims on this basis. [FN37] To establish***731** nonobviousness in such cases, one must show the difficulty and unpredictability of cloning the desired gene. If enough is known about the protein corresponding to the desired gene to permit its preparation in pure form, it is likely that the patent examiner will reject any claims to the protein-encoding DNA sequence on the ground that the invention is obvious in light of known cloning techniques. [FN38]

The Court of Appeals for the Federal Circuit has considered obviousness challenges to the validity of biotech-

nology patent claims in two cases. The earlier of these cases, *Hybritech, Inc. v. Monoclonal Antibodies, Inc.,* [FN39] suggests a more generous attitude toward the validity of the claims than the more recent case, *In re O'Farrell.* [FN40]

In *Hybritech,* the plaintiff held a process patent on a "sandwich assay" for detecting the presence of antigenic substances in fluid samples using monoclonal antibodies. [FN41] The district court held the claims invalid on grounds of obviousness. In doing so, the court relied on prior art showing ways to prepare monoclonal antibodies, and also showing similar assays using conventional polyclonal antibodies. [FN42] The Federal Circuit reversed, noting that the prior art references were no more than "invitations to try monoclonal antibodies in immunoassays" that "do not suggest how that end might be accomplished." [FN43]

Two years later, in *In re O'Farrell,* the Federal Circuit affirmed the PTO's rejection of patent claims to a method for producing proteins in bacterial host cells on grounds of obviousness. [FN44] The claimed method involved inserting the target gene in a plasmid in the middle of the DNA for a bacterial protein, and then introducing the plasmid into the bacterial host. In attempting to express the gene for the bacterial protein, the host would then "read through" to express the target gene, creating a fused ***732** protein that included the amino acid sequence coded for by the target gene. [FN45]

The most significant prior art reference was an article co-authored by two of the three co-inventor patent applicants [FN46] describing the use of a similar technique to introduce a gene coding for a ribosomal RNA into a bacterial host cell. The authors noted evidence that the bacterial host was expressing the foreign gene and suggested that by substituting a gene coding for a protein in lieu of the ribosomal RNA gene, one might be able to cause the bacterial host cell to produce the protein. [FN47] The Federal Circuit agreed with the PTO that this article made the substitution of the gene for a protein obvious to one of ordinary skill in the art at the time the invention was made.

The court rejected the argument of the applicants that in view of the unpredictability of success in the field of molecular biology at the time of the publication, the article at most made the invention "obvious to try." The court noted that the article "contained detailed enabling methodology for practicing the claimed invention, a suggestion to modify the prior art to practice the claimed invention, and evidence suggesting that it would be successful." [FN48] The existence of some uncertainty as to the outcome of developing an invention does not make the invention nonobvious if there is a "reasonable expectation of success." [FN49]

After *O'Farrell* an invention might be nonobvious, even though it is "obvious to try," in three situations: (1) if there is no reasonable expectation of success; (2) if arriving at the invention requires undue experimentation by varying all parameters or trying each of numerous possible choices in the hope of arriving at a successful result, with no indication in the prior art of which parameters are critical or no direction as to which of many possible choices is likely to succeed; or (3) if the prior art merely suggests exploration of a promising field of experimentation and gives only general guidance as to the particular form of the claimed invention or ***733** how to achieve it.

Applying this formula to claims to the DNA sequences in human genes, such inventions are certainly "obvious to try." Moreover, it is increasingly difficult to argue, in light of advances in molecular biology, protein chemistry and cloning techniques, that there is no reasonable expectation of success, especially if the amino acid sequence for the protein is known. Nor can it be argued in most cases that the prior art gives only general guidance as to how to proceed, unless there is some reason why the gene cannot be retrieved using standard techniques. [FN50]

Where standard techniques are used, the only possible line of argument is that cloning involves undue experimentation because it requires screening countless clones for the desired gene. Two recent decisions of the Board of Patent Appeals and Interferences (the Board) considered a similar issue in the context of claims to monoclonal antibodies, reaching opposite results. In *Ex parte Old* [FN51] the applicant claimed monoclonal antibodies for specific human renal tumor agents. The examiner rejected the claims as obvious in view of the existence of polyclonal anti-

bodies for human renal cell antigens and known techniques for preparing monoclonal antibodies. [FN52] The Board reversed, observing that hybridoma technology is an empirical art in which results are unpredictable, thus yielding no "expected" results. [FN53] The following year, a different panel of the Board affirmed the rejection of claims to monoclonal antibodies for fibroblast interferon in *Ex parte Erlich* [FN54] with only passing reference to *Ex parte Old.* The Board found that "once the antigen of interest is selected, the use of that antigen in the known method . . . will result in the expected hybrid cell lines and the specific monoclonal antibodies," and that "[o]ne would have approached this project with a reasonable expectation of success . . . . " [FN55] The Board specifically rejected the argument that the necessity of screening a large number of hybrid cells for antibody production***734** rendered the invention nonobvious, noting that although this step is "tedious and laborious," it is routine in the hybridoma field. [FN56]

Given that the same technology was involved in both cases, it is difficult to reconcile the divergent findings in *Old* and *Erlich.* Nonetheless, in both cases the critical inquiry was whether success was reasonably predictable on the basis of the prior art. Where a gene is cloned successfully using standard techniques, it is likely that the Patent and Trademark Office will conclude that success was reasonably predictable. [FN57] In light of the *Erlich* decision, it is doubtful that an inventor could avoid a nonobviousness rejection by arguing that identifying the correct clone through standard techniques involved a tedious screening effort, given that such screening efforts are routine in the field.

The discovery of the DNA sequence for a human gene may still be nonobvious under *O'Farrell* in a case where the gene could not be retrieved through standard techniques. The inventor who has to develop a new technique to isolate a previously unavailable DNA sequence may be able to claim that sequence as a nonobvious invention, arguing that the prior art merely suggests a promising field of experimentation but does not disclose how to find the sequence. This argument was persuasive to the court in the recent case of *Amgen, Inc. v. Chugai Pharmaceutical Co.* [FN58] In that case the defendant challenged the validity of a claim to a purified and isolated DNA sequence encoding human erythropoietin on grounds, inter alia, that the invention was obvious. The court concluded that the defendant failed to sustain its burden of proof in light of evidence that the probing and screening procedures used by the inventor to isolate the gene were nonobvious. [FN59]

This analysis might seem to confuse the patentability of the DNA sequence itself with the patentability of the nonobvious process of obtaining it. It has long been established that one cannot obtain a patent on an old product merely by developing a new and nonobvious means of obtaining that product. [FN60] Nonetheless, a series of uncontradicted cases have allowed ***735** patents on products that were obviously desirable, but unobtainable under the prior art, to inventors who develop nonobvious means of preparing such products. [FN61] While this result may seem illogical in purely doctrinal terms, [FN62] it makes a certain amount of sense on a practical level. As long as only one means of making the patented product exists, and all relevant activities occur in the United States, it makes little difference whether the patent holder has a monopoly on the product itself or on the only means of making it. [FN63] The practical significance of conferring a patent monopoly on the product itself rather than limiting the inventor to a process patent on a specific means of making the product increases when other means are developed for making the same product. At that point, if the first inventor has a product patent, her patent protection remains intact, but if she is limited to a process patent, she will lose her monopoly position. Thereafter, because of the difficulty of detecting and proving which of several ***736** available means were used to make an unpatented product, it will be difficult to enforce the patent on the original patented process even against those who are in fact using that process. In other words, as a practical matter a patent on the only known means of making an unpatented product may be effective only for as long as it takes someone to develop another means of making the same thing, which may be far less time than the duration of the patent term.

A rule that limits the first inventor to process patent protection may consequently provide a considerably weaker incentive to invest in developing the first means of making an obviously desirable product than a rule that offers product patent protection. Whether the process patent alone would provide an adequate incentive to induce the necessary inventive effort is ultimately an empirical question with an answer that varies from one invention to the next.

Yet the first inventor to develop a means of making an obviously desirable but previously unobtainable product has made an invention that the public may well consider worth the price of a patent monopoly on the product itself. Rather than risk losing valuable inventions by offering too little patent protection in the form of what may eventually become an unenforceable process patent, it may be preferable to offer the higher bounty of a product patent at the outset.

In sum, as the state of knowledge in biotechnology-related fields advances, it is likely that many newly derived DNA sequences will be deemed obvious in light of the prior art, particularly if they are derived using standard techniques. Nonetheless, inventors who develop new and nonobvious means of cloning previously unavailable DNA sequences may be able to satisfy the nonobviousness requirement for patenting the sequences themselves by showing the nonobviousness of the means used to obtain them.

II. POLICY CONSIDERATIONS IN PATENTING HUMAN DNA SEQUENCES

Assuming that some human DNA sequences are in fact patentable under existing patent doctrine, does that outcome make sense? Or would we be better off as a matter of social policy leaving this information in the public domain? Given the importance of this information to the public welfare, might we not better promote its widespread use by leaving it ***737** freely available to all?

At one level these questions are not confined to the patentability of DNA sequences but could as readily be asked about the patent system as a whole. While the patent system is often justified as a means of providing incentives to invest in socially valuable research and development, there are no clear answers to the empirical questions of when these incentives are needed, or how strong the incentives should be to have an optimal impact on behavior. [FN64] A narrower, somewhat easier question to analyze is, assuming that the patent system is an appropriate way of stimulating investment in some areas of research, is there any reason to think that it is a less appropriate way of stimulating research involving DNA sequences in the human genome?

A. Federal Funding for Sequencing the Human Genome

One distinction that might justify denying patent protection for human DNA sequences without calling into question the basis for the patent system as a whole is that the federal government is currently funding research to sequence the human genome. It therefore can be argued that patent incentives are unnecessary to stimulate the development of this information. Moreover, one might argue that allowing patent protection on information generated in part through federal funds forces the public to pay twice for the same invention: first, as taxpayers sponsoring the research, and second, as consumers paying royalties to the patent holder for use of the invention.

There are several reasons for rejecting these arguments. First, the amount of federal funding for the Human Genome Project is trivial compared to the amount of private funding for biotechnology research and development. Current projections for funding once the project is underway are in the range of $200 million per year. [FN65] Amounts allocated to date fall considerably short of that figure. [FN66] This compares to an estimated $1.5 to ***738** $2 billion invested by private industry in biotechnology research and development in 1987. [FN67] Assuming that continued private funding is contingent on the availability of patent protection, [FN68] it is doubtful that federal funding for the Human Genome Project could compensate for the reduction in private incentives for research and development if patent protection were denied.

Second, at this point federal funding is limited to mapping and sequencing the human genome, and the availability of public funds for subsequent research and development to turn this information into useful products and processes is uncertain. [FN69] One might expect that even without continued public funding at this later stage, the free availability of sequence information generated through public funding would promote subsequent research and development better than private control of this information under the patent laws. But some scholars believe that the

incentives provided by patent protection are most important *after* an invention has been made, as a means of stimulating investment in putting patented inventions to practical use, rather than before the invention has been made, as a means of stimulating the initial research necessary to create the invention. [FN70] In the absence of continued public funding, patent incentives may be necessary to stimulate private investment to take its place.

Of course, it does not necessarily follow that private firms will need patent protection on DNA sequences to invest in putting this information to use. Firms might, instead, protect their investments through patents on the innovations they make in the course of putting earlier inventions into use, such as process patents on techniques for making desirable proteins through recombinant DNA technology. But these processes, although ***739** costly, are often considered standard in the art and thus unpatentable. [FN71] Moreover, even when the processes are sufficiently inventive to be patentable, it may be difficult to detect and prove infringement of such process patents. In the absence of effective patent protection for biotechnology processes, some form of product patent protection may be necessary, whether the patented products are DNA sequences, recombinant materials incorporating such sequences, or the proteins they produce. [FN72]

Third, while at one time federal government policy viewed private ownership of inventions made through public funding as contrary to the public interest, [FN73] this is no longer the case. Objections to patent protection for inventions made with government funding today contradict the express policy of the federal government "to use the patent system to promote the utilization of inventions arising from federally supported research or development." [FN74] The 1980 Patent & Trademark Act amendments [FN75] promote the patenting and commercialization of inventions arising out of government-sponsored research by allowing non-profit research institutions and small businesses to retain ownership of all patent rights in such inventions and by allowing large businesses to receive exclusive licenses for specific uses of such inventions. [FN76] The legislative history of these provisions reflects a policy of promoting industrial innovation by "encourag[ing] private industry to utilize government funded inventions through the commitment of the risk capital necessary to develop such inventions to the point ***740** of commercial application." [FN77]

B. Promoting Progress in Basic Scientific Research

A somewhat different line of argument that may come closer to the basis for objections to intellectual property protection held by scientists involved in the Human Genome Project is that, even if commercial development is better served by allowing patent protection, continuing progress in scientific research will be better served by leaving the human genome in the public domain. Information concerning human DNA sequences is vital to the future course of basic research in the biomedical sciences, [FN78] and allowing this information to be controlled by private patent owners could retard scientific progress in these fields. The scientific community operates on a principle of communal ownership of research results rather than private ownership. [FN79] The possibility of obtaining patent rights thus threatens the mechanisms of the scientific community for generating and disseminating new knowledge by hampering communications among scientists and impeding the use of prior research results in subsequent research. [FN80]

I have analyzed this line of argument at length elsewhere [FN81] and will only summarize the analysis here. Since patent protection has traditionally been confined to the practical results of applied research and has been unavailable for basic research discoveries, the implications of patent protection for discoveries that are significant to both basic and applied research are not well understood. While some fears of scientists that patent protection will interfere with the progress of science are well-founded, some are misguided.

Both patent law and scientific norms favor full disclosure of new discoveries to the public. [FN82] Indeed, patent law may be more rigorous in enforcing its disclosure requirements than the scientific community is in enforcing its own disclosure norms. In the long run it is thus unlikely that ***741** patent protection for human DNA sequences will prevent dissemination of this knowledge to the scientific community and the public at large. Indeed, one might expect that less disclosure would occur if patent protection for DNA sequences were denied, inasmuch as inventors

would then be compelled to rely on secrecy to protect their newly discovered sequences.

On the other hand, disclosure through the patent system is likely to occur considerably later than disclosure motivated solely by scientific norms and rewards. Although both the patent law and the scientific community reward priority of invention and thus place a premium on prompt disclosure of new discoveries, patent applicants are likely to publish their discoveries later than scientists who are indifferent to intellectual property rights. One reason for this difference is that some discoveries may be ripe for recognition in the scientific community before they are ripe for patent protection. Yet a scientist who publishes the results of research that has not yet yielded a patentable invention may jeopardize her prospects for obtaining patent protection on inventions emanating from this research in the future because her own publications will become prior art that may be cited against her. [FN83] Scientists who hope to secure patents may therefore defer publication until their research has yielded patentable inventions, thereby slowing down the dissemination of new knowledge to the scientific community.

In theory, once an inventor has made a patentable invention and filed a patent application, she is free to publish her research results without compromising her patent rights. But an inventor who is uncertain about the patentability of her invention might defer publication until a patent actually issues [FN84] in order to preserve the option of protecting the invention through trade secrecy. Given the current backlog of biotechnology patent ***742** applications in the PTO, a patent applicant may have to wait four to five years after the application date before the patent examiner reaches a final decision on whether to issue a patent. [FN85] This particular dimension to the delay in disseminating new information by patent applicants could be ameliorated by greater certainty as to the patentability of DNA sequences, which would make applicants more willing to disclose their inventions before a patent issues. Nonetheless, under patent law as it now stands, there is good reason to fear that inventors whose disclosure decisions are motivated by intellectual property considerations will disclose their discoveries considerably later than scientists who are motivated solely by scientific norms and rewards.

Patent protection may also impede scientific progress even after disclosure occurs if it gives patent holders the power to stop others from using their discoveries in subsequent research. [FN86] In this respect the conflict between the patent system and scientific norms seems intractable: the patent system rests on the premise that scientific progress will best be promoted by conferring exclusive rights in new discoveries, while the research science community has traditionally proceeded on the opposite assumption that science will advance most rapidly if the community enjoys free access to prior discoveries. [FN87]

This conflict could be minimized by exempting the use of patented inventions in research from infringement liability. But although many cases have recognized such an exemption in dicta, the scope of the exemption is unclear. The Court of Appeals for the Federal Circuit has characterized the exemption as "truly narrow," [FN88] suggesting that legislative action may be necessary in order to clarify the rights of researchers to use patented inventions without first obtaining licenses.

Even without an experimental use exemption from infringement liability, holders of patents on human DNA sequences might not enforce their exclusive rights against subsequent researchers. The use of patented DNA ***743** sequences in research laboratories might not come to the attention of patent holders or, if it did, it might not provoke any objections. It may not be worth the trouble to sue a researcher or university for patent infringement, particularly if the research does not threaten the commercial interests of the patent holder. Some patent holders would probably be delighted to see scientists using their sequences in subsequent research, hoping that this research will ultimately enhance the value of their patents.

On the other hand, some patent holders might be reluctant to allow the use of their inventions in research, fearing that subsequent researchers will develop non-infringing substitutes for the patented inventions which would undermine the value of their patents. Such patent holders might be unwilling to offer licenses to researchers, or might charge them exorbitant royalties. But even if most patent holders do not object to the use of their inventions in research or are willing to extend licenses for nominal royalties, the need to contact patent holders and obtain licenses

to use their inventions in research could add significantly to the administrative burdens of researchers in fields where patent protection is widespread.

An experimental use exemption from infringement liability could prevent patents from burdening the progress of research science while still preserving incentives for private investment in research and development in biotechnology. This might be a better solution to the conflict between patent law and scientific norms than denying patent protection entirely in fields where basic science and commercial interests converge.

While there is reason to fear that patent protection for human DNA sequences could cause delays in the publication and dissemination of new knowledge about the human genome and could enable some patent holders to stop the use of their patented sequences in subsequent research, it is not clear that denying patent protection is the most appropriate solution to these problems. So long as newly derived DNA sequences have commercial value, the absence of patent protection might impede the dissemination of information even more by leaving commercial firms with no alternative to secrecy as a means of preserving exclusive rights. The problem of interim secrecy while inventors pursue patent protection could be ameliorated by providing greater certainty as to the patentability of DNA sequences and streamlining administrative procedures in the PTO to expedite the issuance of patents. Moreover, concerns that patent holders might ***744** use their exclusive rights to block the use of their patented sequences in subsequent research would be better met by an appropriately framed experimental use exemption from infringement liability than by denying patent protection entirely.

CONCLUSION

As the Human Genome Project gets under way, some scientists have spoken out against allowing private intellectual property rights in human DNA sequences. Meanwhile, the Patent and Trademark Office has been issuing patents on newly derived human DNA sequences to private parties. While these sequences may satisfy subject matter and novelty requirements for patentability, the validity of some of these patents may still be subject to challenge on grounds of obviousness. Nonetheless, at the very least, it seems likely that DNA sequences whose identification and isolation required the development of new and inventive techniques would be held nonobvious and patentable under present law.

Given the importance of funding from private industry to biomedical research today, it is not clear that patent protection for DNA sequences is a bad thing. The small amounts of federal funding projected for the Human Genome Project cannot be expected to displace private funding in this area. Moreover, even if public funding were sufficient to generate the sequence information itself, the lack of intellectual property rights in DNA sequences might undermine incentives for the private sector to support subsequent research to put this information to practical use. Since 1980, federal law has promoted private exploitation of patent rights in inventions emanating from federally-sponsored research as a means of promoting the development of these inventions.

There is some reason for concern that the pursuit of patent rights in human DNA sequences might interfere with scientific progress. Inventors who seek patent protection might delay publication and dissemination of their research results, and patent holders might use their exclusive rights to stop subsequent research by others. But denying patent protection does not seem to be the best solution to these problems. Indeed, in the absence of patent protection, inventors who are motivated to protect their intellectual property might be even less inclined to publish their results since they would have to rely on secrecy as a means of preserving exclusivity. ***745** Problems of interim secrecy under the patent laws could be ameliorated by increasing certainty as to the availability of patent protection and decreasing delays in the patent office. Concerns about patent holders blocking the use of their inventions in subsequent research might be better met through an experimental use exemption to patent infringement liability than through denying patent protection entirely.

The scientists' objections to intellectual property rights in the human genome undoubtedly rest in part on sym-

bolic considerations. Wary of a public that has voiced strong objections to recombinant DNA research in the past, the scientific community may want to claim for itself the high road of promoting the public welfare over private gain in order to forestall opposition to the Human Genome Project. Scientists would like to think that they are involved in a cooperative effort for the advancement of knowledge and the betterment of humanity, not in a self-interested effort to privatize new knowledge for profit. But this begs the question of how best to promote the advancement of knowledge and the betterment of humanity. If private intellectual property rights in human DNA sequences are indeed inconsistent with these goals, then the human genome should certainly remain in the public domain. But given the substantial and growing dependence of biomedical research on private funding, we should be cautious about assuming that private intellectual property rights will retard progress in these fields.

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[FN1] *See* Norman, *Bush Budget Highlights R&D,* 247 SCIENCE 517 (1990) (reporting increase in funding for Human Genome Project from $87 million in 1990 to $154 million in the Bush Administration's proposed budget for 1991).

[FN2] *See generally Commercialization of Academic Biomedical Research: Hearings Before the Subcomm. on Investigations and Oversight and the Subcomm. on Science, Research and Technology of the House Comm. on Science and Technology,* 97th Cong., 1st Sess. (1981).

[FN3] *See, e.g.,* COMMITTEE ON MAPPING AND SEQUENCING THE HUMAN GENOME OF THE NATIONAL RESEARCH COUNCIL, MAPPING AND SEQUENCING THE HUMAN GENOME 99-100 (1988) [hereinafter NATIONAL RESEARCH COUNCIL COMMITTEE REPORT]; McKusick, *Mapping and Sequencing the Human Genome,* 320 NEW ENG. J. MED. 910, 912 (1989); Arnst, *Scientists Working on World Effort to Map All Human Genes,* REUTERS (June 12, 1989) (NEXIS, Wires Library).

Curiously, some of these scientists have assumed that patent protection for DNA sequence information is not available, and that copyright laws offer the only relevant intellectual property rights. *See, e.g.,* NATIONAL RESEARCH COUNCIL COMMITTEE REPORT, *supra,* at 99-100. In fact, copyright protection for DNA sequences has failed to make its mark outside the scholarly literature. *See* I. COPPER, BIOTECHNOLOGY AND THE LAW § 11.02 (1989); Burk, *Copyrightability of Recombinant DNA Sequences,* 29 JURIMETRICS J. 469 (1989); Goldstein, *Copyrightability of Genetic Works,* BIO/TECHNOLOGY, Feb. 1984, at 138; Kayton, *Copyright in Living Genetically Engineered Works,* 50 GEO. WASH. L. REV. 191 (1982).

[FN4] *See, e.g.,* U.S. Patent 4,370,417, 1026 Official Gazette Pat. Off. 1315 (Jan. 25, 1983) (claiming DNA sequence for plasminogen activator protein); U. S. Patent 4,703,008, 1083 Official Gazette Pat. Off. 2038 (Oct. 27, 1987) (claiming DNA sequence for erythropoietin); U.S. Patent 4,713,332, 1085 Official Gazette Pat. Off. 1386 (Dec. 15, 1987) (claiming DNA sequence for human T cell antigen receptor); U.S. Patent 4,757,006, 1092 Official Gazette Pat. Off. 878 (July 12, 1988) (claiming recombinant vectors containing DNA sequence for human factor VIII:C).

[FN5] 35 U.S.C. § 154 (1988).

[FN6] 35 U.S.C. § 271 (1988); R. HARMON, PATENTS AND THE FEDERAL CIRCUIT 110-11 (1988).

[FN7] 35 U.S.C. § 112 (1988).

[FN8] *See* United States v. Dubilier Condenser Corp., 289 U.S. 178, 186-87 (1933) (disclosure and the consequent

benefits to the community are consideration for the patent); Grant v. Raymond, 31 U.S. (6 Pet.) 218, 247 (1832) (disclosure is the preliminary requirement to issuing a patent).

[FN9] Application of Argoudelis, 434 F.2d 1390, 1394 (C.C.P.A. 1970) (Baldwin, J. concurring).

[FN10] 35 U.S.C. § 101 (1988). The requirement that an invention be "new" is elaborated upon in 35 U.S.C. § 102 (1988).

[FN11] *See* Eisenberg, *Proprietary Rights and the Norms of Science in Biotechnology Research*, 97 YALE L.J. 177, 186-87 (1987) [hereinafter Eisenberg, *Rights and Norms*].

[FN12] 35 U.S.C. § 103 (1988); *see also* Graham v. John Deere Co., 383 U.S. 1, 13-19 (1966) (interpreting § 103 as a codification of case law requiring an independent determination of nonobviousness as a prerequisite to patentability).

[FN13] 33 U.S. 127 (1948).

[FN14] An illustrative claim from the patent reads:

> An inoculant for leguminous plants comprising a plurality of selected mutually non-inhibitive strains of different species of bacteria of the genus Rhizobium, said strains being unaffected by each other in respect to their ability to fix nitrogen in the leguminous plant for which they are specific.

Id. at 128 n.1.

[FN15] *Id.* at 130 (citation omitted).

[FN16] *Id.* at 131. Douglas rejected the argument that the patent holder had gone beyond discovering a law of nature to make a new and different composition of non-inhibitive strains, noting that "that aggregation of species fell short of invention within the meaning of the patent statutes." This last remark suggests that the problem with the patent was not that the claimed invention lacked novelty or fell outside the categories of statutory subject matter as a product of nature, but rather that the invention was obvious. Indeed, Professor Chisum argues that the claimed invention was not a true product of nature because the claimed mixed culture did not exist in a natural form, and that the decision "is perhaps best viewed as an interpretation of the nonobviousness or 'invention' requirement, and not of the statutory classes of subject matter." 1 D. CHISUM, PATENTS § 1.02[7] (1990). But much of the language of the opinion supports a broader prohibition on patenting "products of nature," even in novel combinations.

[FN17] *cf.* Amgen, Inc. v. Chugai Pharmaceutical Co., 13 U.S.P.Q.2d 1737, 1759 (D. Mass. 1989) (noting that the DNA sequence encoding human erythropoietin "is a nonpatentable natural phenomenon 'free to all men and reserved exclusively to none,"' although a "purified and isolated" DNA sequence encoding the same protein might be patentable).

[FN18] 447 U.S. 303 (1980).

[FN19] *Id.* at 306 n.3.

[FN20] *Id.* at 308-09.

[FN21] *Id.* at 310. One could quarrel with this distinction. Both patents claimed combinations of naturally occurring elements, and in both cases the combination itself did not exist in nature.

[FN22] *Id.*

[FN23] *Id.* at 309 (quoting S. REP. NO. 1979, 82d Cong., 2d Sess. 5 (1952) and H.R. REP. NO. 1923, 82d Cong., 2d Sess. 6 (1952)).

The Patent and Trademark Office relied on this language in deciding to extend patent protection to "non-naturally occurring non-human multicellular living organisms, including animals." *See Nonnaturally Occurring Non-Human Animals Are Patentable Under § 101,* 33 Pat. Trademark & Copyright J. (BNA) No. 927, at 664 (Apr. 23, 1987).

[FN24] *See, e.g.,* U.S. Patent 4,757,006, 1092 Official Gazette Pat. Off. 878 (July 12, 1988). This patent claims, inter alia:

> 1. An isolated recombinant vector containing DNA coding for human factor VIII:C, comprising a polydeoxyribonucleotide having the [following] sequence:
>
> 4. A non-human recombinant expression vector for human factor VIII:C comprising a DNA segment having the [following] sequence:
>
> 5. A transformed non-human mammalian cell line containing the expression vector of claim 4.

[FN25] A cloned gene may in fact have a somewhat different DNA sequence than the corresponding chromosomal DNA sequence from which it was transcribed. This is because cloned genes generally are derived from the messenger RNA corresponding to the desired gene rather than obtained directly from the chromosomes of a cell. Chromosomal DNA includes regulatory sequences and extraneous information or "introns" that do not appear in the messenger RNA from which complementary DNA (cDNA) strands are made. Assuming that a sequence identical to that of the cDNA clone does not occur naturally in human cells without any intervention, then the cDNA sequence itself might be sufficiently distinct from the naturally occurring DNA sequence to be a new composition of matter rather than an unpatentable product of nature. *See generally* NATIONAL RESEARCH COUNCIL COMMITTEE REPORT, *supra* note 3, at 13-19, 57-58.

[FN26] *See, e.g.,* Amgen, Inc. v. Chugai Pharmaceutical Co., 13 U.S.P.Q.2d 1737, 1759 (D. Mass. 1989), upholding the validity of claims of U.S. Patent 4,703,008, *supra* note 4, to purified and isolated DNA sequences as well as recombinant vectors and host cells used to produce erythropoietin (EPO). Claim 2 of that patent reads as follows:

> 2. A purified and isolated DNA sequence consisting essentially of a DNA sequence encoding human erythropoietin.

The court rejected plaintiff's arguments that the claimed invention was "the DNA sequence encoding human EPO," noting that sequence is a "nonpatentable natural phenomenon." *Amgen,* 13 U.S.P.Q.2d at 1759. Instead, the court construed the claim as limited to the "purified and isolated" DNA sequence. *Id.*

[FN27] *See, e.g., In re* Bergstrom, 427 F.2d 1394 (C.C.P.A. 1970) (pure prostaglandins isolated from nature patentable as new products); Parke-Davis & Co. v. H.K. Mulford & Co., 189 F. 95 (S.D.N.Y. 1911), *aff'd,* 196 F. 496 (2d Cir. 1912) (purified adrenalin composition patentable in view of fact that patent holder was the first to make adrenalin available for therapeutic use by removing it from the other gland-tissue in which it was found); Kuehmsted v. Farbenfabriken, 179 F. 701 (7th Cir. 1910), *cert. denied,* 220 U.S. 622 (1911) (upholding validity of patent on acetyl salicylic acid to first inventor to develop process for producing it in sufficiently pure state to render it therapeutically available). *See also In re* Bergy, 563 F.2d 1031 (C.C.P.A. 1977), *vacated sub nom.* Parker v. Bergy, 438 U.S. 902 (1978), *on remand, In re* Bergy, 596 F.2d 952 (C.C.P.A.), *cert. granted sub nom.* Parker v. Bergy, 444

U.S. 924 (1979), *vacated and remanded with instructions to dismiss as moot sub nom.* Diamond v. Chakrabarty, 444 U.S. 1028 (1980) (biologically pure culture of the microorganism *streptomyces vellosus* patentable since it did not exist in nature in a pure form and could be produced only under carefully controlled laboratory conditions).

[FN28] 253 F.2d 156 (4th Cir. 1958).

[FN29] *Id.* at 161 n.6.

[FN30] *Id.* at 161-62.

[FN31] 427 F.2d 1394, 1401 (C.C.P.A. 1970).

[FN32] *Id.* at 1401-02. *cf.* Diamond v. Chakrabarty, 447 U.S. 303, 310 (1980) (noting that Chakrabarty created an organism with properties possessed by no naturally occurring bacteria and "having the potential for significant utility").

[FN33] 563 F.2d 1031 (C.C.P.A. 1977), *vacated sub nom.* Parker v. Bergy, 438 U.S. 902 (1978), *on remand, In re* Bergy, 596 F.2d 952 (C.C.P.A.), *cert. granted sub nom.* Parker v. Bergy, 444 U.S. 924 (1979), *vacated and remanded with instructions to dismiss as moot sub nom.* Diamond v. Chakrabarty, 444 U.S. 1028 (1980).

[FN34] 563 F.2d at 1035.

[FN35] 35 U.S.C. § 103 (1988). *See, e.g., Ex parte* Allen, 2 U.S.P.Q.2d 1425 (PTO Bd. Pat. App. & Int. 1987) (affirming rejection of claim to polyploid oysters on ground that invention was obvious under section 103, although disapproving examiner's rejection of same claim on ground that claimed oysters are living entities and "controlled by laws of nature" and therefore outside scope of patentable subject matter under section 101).

To determine whether an invention is obvious within the meaning of section 103, it is necessary to consider the scope and content of the prior art, the differences between the prior art and the claims at issue, and the level of ordinary skill in the pertinent art. Graham v. John Deere Co., 383 U.S. 1, 17 (1966).

[FN36] *See, e.g.,* Merck & Co. v. Olin Mathieson Chem. Corp., 253 F.2d 156, 159-61 (4th Cir. 1958) (reviewing in detail the efforts of the inventors to isolate and purify vitamin B_{12} and noting that the prior art did not suggest use of the materials from which inventors ultimately were able to purify vitamin B_{12}).

[FN37] *See* Murashige, *Section 102/103 Issues in Biotechnology Patent Prosecution,* 16 AIPLA Q.J. 294, 297 (1988-89); Wiseman, *Biotechnology Patent Practice -- A Primer,* 16 AIPLA Q.J. 394, 409-10 (1988-89).

[FN38] Murashige, *supra* note 37, at 297-99.

[FN39] 802 F.2d 1367 (Fed. Cir. 1986), *cert. denied,* 480 U.S. 947 (1987).

[FN40] 853 F.2d 894 (Fed. Cir. 1988).

[FN41] 802 F.2d at 1370.

[FN42] *Id.* at 1372-74

[FN43] *Id.* at 1380. The court also cited the commercial success of the plaintiff's assays and their unexpected advantages over previously available assays as secondary factors indicating the nonobviousness of the invention. *Id.* at

1382-84.

[FN44] 853 F.2d 894 (Fed. Cir. 1988).

[FN45] *Id.* at 895 (quoting Patent Application No. 180,424).

[FN46] *Id.* at 899 & n.8. An inventor's own printed publications may be cited as prior art against her if they disclose or make obvious her subsequently claimed inventions. *See, e.g.*, Massachusetts Inst. of Tech. v. AB Fortia, 774 F.2d 1104, 1108-09 (Fed. Cir. 1985).

[FN47] 853 F.2d at 900-01.

[FN48] *Id.* at 902.

[FN49] *Id.* at 903-04.

[FN50] *See* Murashige, *supra* note 37, at 297-98.

[FN51] 229 U.S.P.Q. 196 (PTO Bd. App. & Int. 1985).

[FN52] *Id.* at 199-200.

[FN53] *Id.* at 200. In dissent, Examiner-in-Chief Merker remarked that "[t]he application of admittedly known standard techniques to admittedly known renal cancer cell lines to produce expected hybridomas which produce expected monoclonal antibodies, . . . while laudatory, does not give rise to a patentable invention." *Id.* at 200.

[FN54] 3 U.S.P.Q.2d 1011 (PTO Bd. Pat. App. & Int. 1986).

[FN55] *Id.* at 1015.

[FN56] *Id.* at 1016.

[FN57] *See* Wiseman, *supra* note 37, at 409-10.

[FN58] 13 U.S.P.Q.2d 1737, 1764-69 (D. Mass. 1989).

[FN59] *Id.* at 1767-69.

[FN60] Buono v. Yankee Maid Dress Corp., 77 F.2d 274, 279 (2d Cir. 1935); 2 D. CHISUM, *supra* note 16, at § 5.04[8].

[FN61] *See, e.g., In re* Irani, 427 F.2d 806 (C.C.P.A. 1970) (reversing rejection of patent on crystalline compound ATMP on ground that it would not have been obvious how to make such a product under prior art); Shaw v. E.B. & A.C. Whiting Co., 417 F.2d 1097 (2d Cir. 1969), *cert. denied,* 397 U.S. 1076 (1970), *reh'g denied,* 398 U.S. 954 (1970) (upholding validity of product patent on artificial filaments with cruciform shape and linear orientation of molecules on ground that it was not obvious in prior art how to make such a product); *In re* Pilkington, 411 F.2d 1345 (C.C.P.A. 1969) (reversing rejection of product claims to distortion-free glass in application filed by inventor of lead flotation process of making such glass in view of novelty of product and nonobviousness of manner of mak-

ing it); *In re* Cofer, 354 F.2d 664 (C.C.P.A. 1966) (reversing rejection of product claims to "high purity diepoxide" to applicant who developed a patentable process of making product, notwithstanding unsuccessful attempts to recover same product in prior art, because prior art failed to disclose means of making product).

[FN62] Chisum criticizes the cases cited *supra* in note 61 for failing to determine the obviousness of the product independently from the obviousness of the process for making it. 2 D. CHISUM, *supra* note 16, at § 5.04[8].

[FN63] The difference was somewhat greater at the time of the decisions cited *supra* in note 61, at least when the product could be made abroad. Until 1988, it did not constitute infringement of a U.S. patent to use a patented process outside the country and then import the product of that process into the United States for sale. So long as the inventor did not make, use, or sell the patented process in the United States, there was no patent infringement. The patent holder's only remedy was to prevent importation of the product made by the patented process under § 337(a) of the Tariff Act of 1930, ch. 497, 46 Stat. 590 (codified at 19 U.S.C. § 1337(a) (1988)). On the other hand, if the inventor held a product patent, sale of the product itself in the U.S. would constitute infringement regardless of where (or how) the product was made. This gap in process patent protection was largely remedied with passage of the Omnibus Trade and Competitiveness Act of 1988, Pub. L. No. 100-418, 102 Stat. 1107 (1988), which added a new section 271(g) to the Patent Act providing, with certain qualifications, that, "Whoever without authority imports into the United States or sells or uses within the United States a product which is made by a process patented in the United States shall be liable as an infringer, if the importation, sale, or use of the product occurs during the term of such process patent." 35 U.S.C. § 271(g) (1988).

[FN64] *See generally* Eisenberg, *Patents and the Progress of Science: Exclusive Rights and Experimental Use,* 56 U. CHI. L. REV. 1017, 1021-46 (1989) [[[hereinafter Eisenberg, *Patents and Progress*].

[FN65] *See* Koshland, *Sequences and Consequences of the Human Genome,* 246 SCIENCE 189 (1989); NATIONAL RESEARCH COUNCIL COMMITTEE REPORT, *supra* note 3, at 90.

[FN66] McKusick, *supra* note 3, at 912 ($18 million for fiscal year 1988 and $47 million for fiscal year 1989); Norman, *supra* note 1, at 517 ($87 million for fiscal year 1990).

[FN67] OFFICE OF TECHNOLOGY ASSESSMENT, U.S. CONGRESS, NEW DEVELOPMENTS IN BIOTECHNOLOGY: U.S. INVESTMENT IN BIOTECHNOLOGY -- SPECIAL REPORT 80 (1988) [[[hereinafter INVESTMENT IN BIOTECHNOLOGY]. Unfortunately, the OTA figures do not supply a breakdown of the type of research and development funded by these companies.

[FN68] This, of course, is an unanswered empirical question. *See generally* Eisenberg, *Patents and Progress, supra* note 64, at 1031-33 and sources cited therein (describing attempts in economics literature to assess impact of patent laws on R&D decisions); *see also* INVESTMENT IN BIOTECHNOLOGY, *supra* note 67, at 101-03 (concluding that uncertainty over patent protection will influence the R&D strategy of many companies).

[FN69] Federal funding for biomedical research generally has been hard to come by in recent years. *See* Palca, *Hard Times at NIH,* 246 SCIENCE 988 (1989).

[FN70] *See* Eisenberg, *Patents and Progress, supra* note 64, at 1036-44 and sources cited therein.

[FN71] *See In re* Durden, 763 F.2d 1406 (Fed. Cir. 1985) (affirming rejection of claims to obvious process of using novel and nonobvious starting materials to produce novel and nonobvious end products); *In re* Albertson, 332 F.2d 379 (C.C.P.A. 1964) (same). *But cf. In re* Mancy, 499 F.2d 1289 (C.C.P.A. 1974) (upholding patentability of claim to use of old culture techniques to produce old product using new strain of bacteria in view of prior unavailability of starting material); *In re* Kuehl, 475 F.2d 658 (C.C.P.A. 1973) (upholding patentability of claim to process of using

novel material, notwithstanding that prior art disclosed identical process using similar but patentably different materials, noting that obviousness of process must be determined without reference to knowledge of new materials). For an effort to reconcile these cases, see Wiseman, *supra* note 37, at 410-11.

[FN72] Patents on purified proteins may offer particularly broad protection. In infringement litigation in the recombinant DNA industry, courts have construed patent claims directed to purified proteins as extending to the same proteins produced through recombinant DNA technology. *See* Amgen, Inc. v. Chugai Pharmaceutical Co., 706 F. Supp. 94 (D. Mass. 1989); Scripps Clinic & Research Found. v. Genentech, Inc., 666 F. Supp. 1379 (N.D. Cal. 1987), *modified in* 678 F. Supp. 1429 (N.D. Cal. 1988), *claims held invalid in* 707 F. Supp. 1547 (N.D. Cal. 1989).

[FN73] *See* Eisenberg, *Rights and Norms, supra* note 11, at 181-82 and sources cited therein.

[FN74] 35 U.S.C. § 200 (1988).

[FN75] Pub. L. No. 96-517, 94 Stat. 3015, 3019-29 (1980) (codified at 35 U.S.C. §§ 200-211 (1988)).

[FN76] 35 U.S.C. § 202 (1988).

[FN77] H.R. REP. NO. 1307, 96th Cong., 2d Sess. 3 (1980), *reprinted in* 1980 U.S. CODE CONG. & ADMIN. NEWS 6460, 6462.

[FN78] *See* NATIONAL RESEARCH COUNCIL COMMITTEE REPORT, *supra* note 3, at 26-33.

[FN79] Eisenberg, *Patents and Progress, supra* note 64, at 1046-66 and sources cited therein.

[FN80] *See* Eisenberg, *Rights and Norms, supra* note 11.

[FN81] *See generally id.;* Eisenberg, *Patents and Progress, supra* note 64.

[FN82] *See* Eisenberg, *Rights and Norms, supra* note 11, at 181-84, 197-205, 207-17.

[FN83] Recall that this happened to the inventors in *In re O'Farrell. See supra* notes 44-49 and accompanying text.

[FN84] Patent applicants who simultaneously seek foreign patent protection will not be able to keep their inventions secret for this long because the patent laws of other nations typically provide for publication of a pending patent application at a specified time after filing and prior to issuance of the patent. For example, if an applicant seeks international patent protection under the Patent Cooperation Treaty or the European Patent Convention, the application will be published 18 months after the filing date. Patent Cooperation Treaty, June 19, 1970, art. 21, 28 U.S.T. 7647, 7666-67, T.I.A.S. No. 8733, at 7666-67; European Patent Convention, Oct. 5, 1973, art. 93, *translated in* K. HAERTEL, EUROPEAN PATENT CONVENTION 19, 62-63 (1980), *reprinted in* 78 PAT. & TRADEMARK REV. 31, 39 (1980).

[FN85] *See* Crawford, *Patent Claim Buildup Haunts Biotechnology,* 239 SCIENCE 723 (1988).

[FN86] The issues addressed in text are more fully explored in Eisenberg, *Rights and Norms, supra* note 11, at 217-26 and Eisenberg, *Patents and Progress, supra* note 64.

[FN87] For an analysis of the underlying logic of each of these viewpoints, *see* Eisenberg, *Patents and Progress, supra* note 64, at 1024-66.

[FN88] Roche Prods., Inc. v. Bolar Pharmaceutical Co., 733 F.2d 858, 863 (Fed. Cir. 1984), *cert. denied sub nom.* Bolar Pharmaceutical Co. v. Roche Prods., Inc., 469 U.S. 856 (1984).

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